

# **A STUDY OF DIASTOLIC FUNCTION IN TYPE II DIABETIC MELLITUS PATIENTS BY CONVENTIONAL ECHO DOPPLER AND TISSUE DOPPLER IMAGING (TDI)**

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# INTRODUCTION

Diabetes may be defined as a disturbance of intermediary metabolism manifesting as chronic sustained hyperglycaemia primarily due to either an absolute or relative lack of insulin. This may be accompanied by other biochemical disorders.

The metabolic deregulation associated with DM causes secondary pathophysiologic changes in the multiple organ systems that impose tremendous burden on the health care system. With increasing incidence worldwide, DM is likely to continue as a leading cause of morbidity and mortality for the foreseeable future.

Two broad categories of DM are designated as Type I and Type II. Type I DM results from auto immune  $\beta$ -cell destruction which leads to insulin deficiency. Type II DM is a heterogeneous group of disorder usually characterised by variable degrees of insulin resistance, impaired insulin secretion and increased glucose production.

## CRITERIA FOR THE DIAGNOSIS OF DIABETES MELLITUS

- Symptoms of diabetes (Polyurea, polydipsia, weight loss) plus random blood glucose concentration  $\geq 200$  mg/dl.

or

- Fasting blood glucose  $\geq 126$  mg/dl.

or

- Two hour plasma glucose  $\geq 200$  mg/dl during an oral glucose tolerance test.

In the absence of unequivocal hyperglycaemia and acute metabolic decompensation these criteria should be confirmed by repeat testing on a different day.

Diastolic abnormalities have been observed in patients with DM. Impaired augmentation of LVEF during exercise occurs in upto 40% of patients. (5) Diastolic dysfunction and abnormal systolic reserve during exercise result from DM. (6) The association of DM to coronary artery disease and hypertension is well known.

So, early recognition of heart disease in diabetes is a desirable goal. Diastolic dysfunction, one of the earliest manifestations can be easily assessed by tissue doppler imaging.

## **AIM OF STUDY**

Diastolic dysfunction is considered the earliest manifestation of diabetes mellitus. The existence of diabetic cardiomyopathy independent atherosclerotic and hypertensive heart disease has been established in adult population.(7)

There is also some controversy over the existence of diabetic cardiomyopathy. So keeping these things in mind, the aim of study is to determine whether diastolic dysfunction exists in an asymptomatic diabetic or not.

Both conventional echocardiography and Tissue Doppler Imaging (TDI) were used to evaluate diastolic function. There are several studies which show that TDI can diagnose diastolic dysfunction earlier than conventional echo-doppler. So, the most important part of the study is to compare both studies. (Conventional Echo & TDI)

Early diagnosis of diastolic dysfunction is a desirable goal. Early diagnosis leads to early intervention which saves the individual from the long term effects of DM. TDI method that help in the early diagnosis of diastolic dysfunction in diabetes is a welcome addition to the diagnostic armamentarium.

## REVIEW OF LITERATURE

The role left ventricular (LV) diastolic dysfunction in health and disease is not yet understood fully. This is because diastole is a complex phenomenon consists of several phases that encompass the relaxation and then filling of ventricles (8,9). Physical examination, ECG, and chest radiographs are unreliable in making the diagnosis of LV diastolic dysfunction in most individuals, and invasive measurements of cardiac pressures, rates of LV relaxation, and LV compliance are costly, clinically impracticable as they carry increased risk and require special catheters and software analysis programmes (10).

One of the first attempts to explain ventricular filling was provided by Galen in 100 BC who proposed that the heart is filled by dilatation of the right ventricle. In 1628, William Harvey recognised the heart was a central pump in circulatory system containing arteries and veins. Diastole was largely ignored as simply the interval in which the cardiac chambers passively filled in between each pumping cycle.

Gradually clues emerged that LV diastolic dysfunction alone can cause symptoms and that diastolic and systolic functions were interrelated. An important discovery was the Frank-Starling mechanism whereby LV end diastolic volume help regulate LV stroke volume on a beat to beat basis. Another landmark observation was made by KATZ, who observed that after mitral valve opening in mammalian hearts LV pressure continues to decrease while volume is increasing, thereby demonstrating that the heart acts as suction pump.

With the advent of cardiac catheterisation in the 1960s, the study of cardiovascular biomechanics accelerated. Although most research continued to

focus on LV systolic function, cardiac diseases with thickened and non compliant ventricles were reported. Soon, angiographic differences in LV filling patterns between normal and patients with various heart diseases were noted (11).

In mid-1980s, echocardiographic studies helped show that 20 to 40% of patients with symptoms of CHF had normal LV ejection fraction and possibly diastolic dysfunction as the etiology. Because of the difficulties in quantitating individual LV diastolic properties, the clinical study of LV diastolic dysfunction proceeded slowly. In 1982, the use of PW Doppler mitral flow velocities to study LV filling was described. Easy to use, noninvasive nature and ability to study changes in LV filling after interventions made this technique to revolutionise the study of LV diastolic dysfunction. Tissue Doppler imaging is a recently developed ultrasound technique that has underlying physics and principles similar to those of conventional PW spectral Doppler.

Heart disease was thought to be associated with diabetes as early as 1882, when Vergerely recommended testing the urine of patients with angina for glucose. The association of diabetes to coronary artery disease and heart failure is well known. The question whether diabetes itself, distinct from CAD and hypertension, results in dilated cardiomyopathy remains controversial.

In the 35 to 64 year old Framingham Cohort, diabetes increased the risk congestive heart failure in men four fold, and in women eightfold, even after adjustment for blood pressure, age, cholesterol, weight and a history of CAD (12). The more recent Washington DC dilated cardiomyopathy study used case control analysis to determine that there was an association between diabetes and idiopathic cardiomyopathy (13). Furthermore various groups have reported diastolic abnormalities using various parameters including prolonged IVRT and abnormal



transmitral flow velocities. Increased echodensity has also been reported despite normal wall thickness(14).

Recently SARAIVA ET AL, have studied diastolic dysfunction in diabetic patients by conventional echo and tissue Doppler imaging (TDI) methods (15).

Similar studies has also been done by many authors.

Boyer ET AL studied the prevalence of ventricular diastolic dysfunction in asymptomatic normotensive patients with diabetes melliton (16).

Vinereanu ET AL studied the subclinical left ventricular dysfunction in asymptomatic patients with type II DM related to serum lipids and glycated haemoglobin (17).

Poirier ET AL studied Diastolic dysfunction in normotensive men with well controlled Type II diabetes (19).

The guidelines for the diagnosis of diastolic dysfunction was issued by European Study Group on Diabetic Heart Failure (18).

## **OVERVIEW OF DIABETES MELLITUS, DIASTOLOGY AND DIASTOLIC DYSFUNCTION**

### **DIABETES MELLITUS**

Diabetes is the seventh leading cause of death in the west, with much of that mortality a result of cardiovascular disease. A two to four-fold excess in mortality due to coronary artery disease (CAD) among individuals with diabetes has been noted in a number of prospective studies. Diabetes also increased the risk of severe carotid atherosclerosis and mortality from stroke increased almost three fold in patients with diabetes. Both type I and type II diabetes are therefore powerful and independent risk factors for CAD, stroke and peripheral arterial disease.

The prevalence of type II diabetes which accounts for 90% of all cases of diabetes is increasing world over. This is due to advancing age of population, improved screening and detection and increase in risk factors such as obesity and physical inactivity.

Life expectancy is shortened, with diabetic males living on an average 9.1 years less and diabetic females living 6.7 years less than their non diabetic counterparts (20).

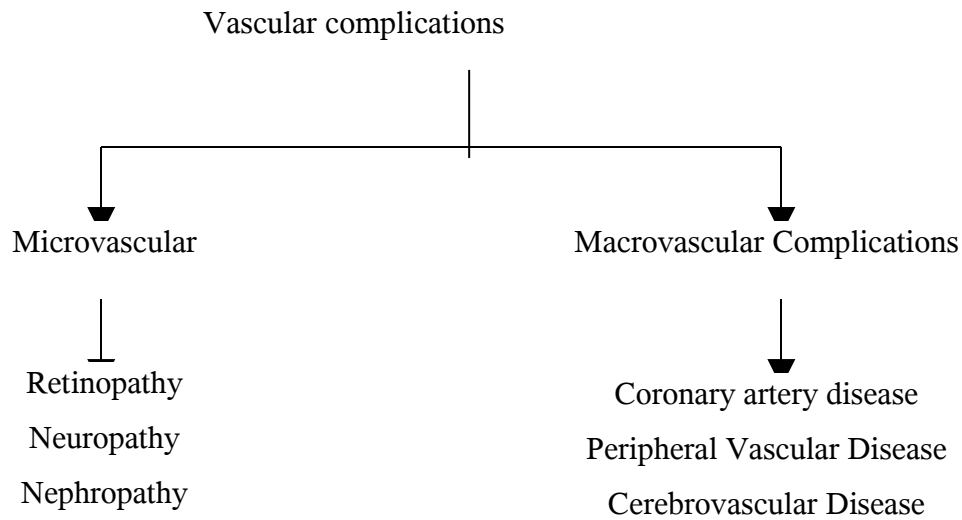
Haffner and colleagues examined the mortality among 1000 persons with Type II DM and 1300 subjects without diabetes and found that mortality of those with diabetes was similar to that for those without diabetes who had a myocardial infarction (MI) (21). This data suggest that caregivers should treat individuals with type II diabetes as if they have experienced an MI. Malmberg et al evaluated the findings of OASIS (organisation to assess strategies for ischaemic syndromes)

registry and found that patients with diabetes hospitalised for unstable angina or non - Q MI had the same long term morbidity and mortality as patients without diabetes with established cardiovascular disease (22).

Many of these patients with type II diabetes have several of these risk factors for CAD. The term METABOLIC SYNDROME was first used by Gerald Reaven in 1988 to describe the clustering of risk factors including hypertension, dyslipidaemia, hyperglycaemia and insulin resistance. The National Cholesterol Education Program Adult Treatment Panel III (ATP III) guidelines for cholesterol management in 2001 recognised that the metabolic syndrome is a collection of risk factors mentioned above as well as abdominal obesity.

The increased risk of cardio vascular disease in diabetics is partly explained by clustering of risk factors, including dyslipidaemia, hypertension, hyperglycaemia, hyper insulinaemia and prothrombotic factors.

## Chronic Complications in DM



### Non Vascular Complications

Gastroparesis, sexual dysfunction and skin changes.

The risk of chronic complications increases as a function of the duration of DM.

Since Type II DM may have a long asymptomatic period of hyperglycaemia, many individuals with type II DM have complications at the time of diagnosis.

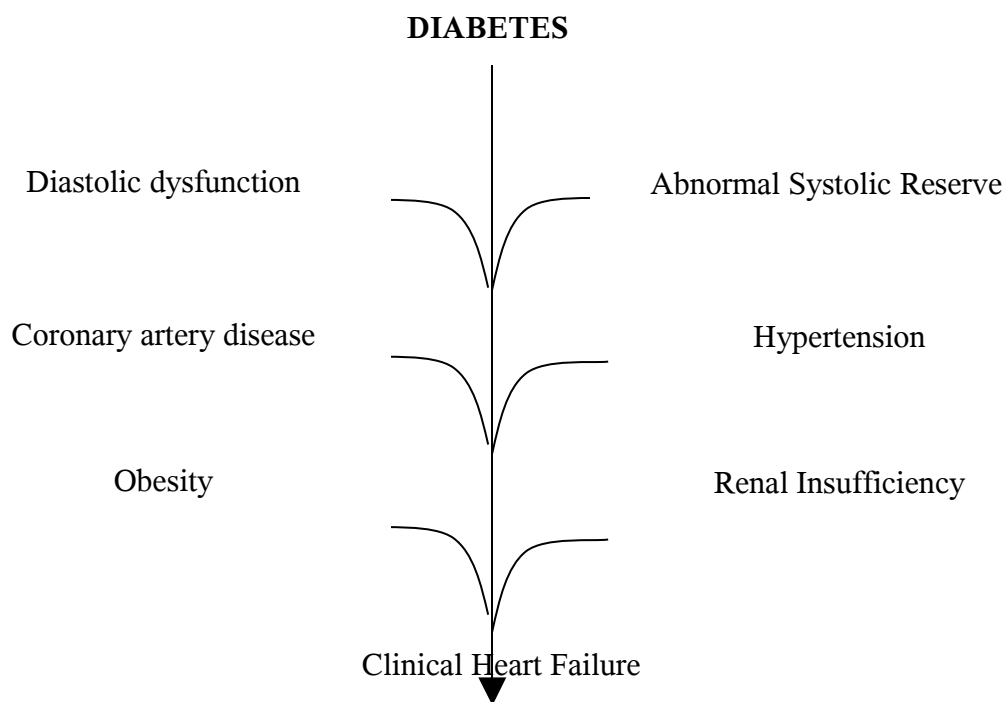
### Congestive Heart Failure

Individuals with DM have increased incidence of congestive cardiac failure. The etiology of this abnormality is probably multifactorial and include factors like myocardial ischaemia from atherosclerosis, hypertension and myocardial cell dysfunction secondary to chronic hyper glycaemia.

### Diabetic Cardiomyopathy

Diabetic Cardiomyopathy is defined as heart failure in the absence of identifiable etiology. In the Framingham heart study few patients with heart failure did not have CAD/hypertension or RHD. The term diabetic cardiomyopathy was first coined by Rubler in 1972.

### MECHANISMS LEADING TO HEART FAILURE IN DM



Diastolic dysfunction and abnormal systolic reserve during exercise may result from Diabetes.

The diagnosis of diabetic cardiomyopathy is sometimes invoked when a patient with diabetes has evidence of heart failure in the absence of identifiable etiology. One of the difficulties in making this diagnosis is lack of definite pathological findings so that differentiation from DCMP remains problematic. The diagnosis of diabetic cardiomyopathy was suggested almost 30 years back. Parelleling the incidence of CAD in patients with diabetes is the incidence of heart

failure. Heart failure is a frequent clinical manifestation of the end stage of cardiovascular complications that affects the patients with DM. Framingham heart study was the first study that showed the risk of symptomatic heart failure with increased 2.4 - fold incidence in men with diabetes and five fold in women with diabetes. Hypertension occurs in 40% to 60% of patients with type II DM. Hypertension is the most common cause of heart failure in patients with DM after CAD, amounting to 25% of the cases.

Pathologically post mortem studies of patients with diabetic cardiomyopathy have revealed that they have features similar to those of patients with other forms of non ischaemic cardiomyopathy. This include myocyte hypertrophy, interstitial fibrosis and infiltration with periodic Acid schiff stain positive materials with coronary arterioles having thickened basement membrane as well as the presence of intramyocardial microangiopathy. Theories abound regarding mechanism or mechanisms underlying diabetic cardiomyopathy. These include both cellular and molecular perturbations, as well as metabolic abnormalities.

Calcium homeostasis may be altered and has been reported in various animal models of DM, suggesting a diminished but prolonged increase in the intracellular calcium concentration.

Hyperglycaemia increases calcium activated signalling through protein kinase C which in turn may result in cardiac dysfunction. Abnormalities in myofibrillar proteins including altered phosphorylation of troponin I and myosin light chains may also play a role in diabetes associated impairment of contractile function (23). Advanced glycosylation result in abnormal collagen cross-linking, which may contribute to decreased compliance and in turn to diastolic dysfunction.

In the United Kingdom Prospective Diabetes Study (UKPDS) the incidence

of heart failure correlated with the extent of hyperglycaemia. Myocardial fibrosis underlies the pathologic hypertrophy and dysfunction that are observed in Heart failure.

### **Pathogenesis of Heart failure in DM**

Increasing blood glucose concentration is an independent and continuous risk factor for the cardiovascular disease. The progressive relationship between glucose levels and cardiovascular risk begins at less than the glucose threshold that is required for the clinical diagnosis of diabetes. The risk of heart failure increases by 15% per 1% increase in HB-A1c in individuals who do and do not have known diabetes. Hyperglycaemia alters protein kinase C, (PKC) increases oxidative stress and up regulate the activity of Angiotensin converting Enzyme (ACE) and other compounds of RAAS, which contributes to the development of cardiomyopathy.

### **Molecular Mechanisms**

PKC has been linked closely to the mechanism that underlies hyperglycaemia induced biochemical alterations, persistent PKC activation results from chronic hyperglycaemia may lead to alterations in cell growth and function by way of PKC dependent phosphorylation of myocardial and skeletal muscle enzymes and proteins that may affect muscle contractility, gene expression and growth. PKC may interfere with contractile proteins troponin T, Troponin - I troponin - Tropomyosin complex and troponin-C proteins as well as inhibition of  $\text{Ca}^{++}$  activated myofibrillar actomyosin  $\text{Mg}^{++}$  ATPase activity and contractility.

ACE in particular may account for development of abnormalities that

contribute to the development of diabetic cardiomyopathy. The increase in ACE activity in diabetics may be direct consequence of glucose mediated activation of PKC.

The presence of DM alters the way the myocardium uses lipids in general and FFA in particular. The normal heart uses fatty acids for approximately 70% of its energy sources. In diabetic heart there is a greater reliance on fatty acid oxidation. There is a depression of glucose oxidation in the heart during diabetes that probably is due to the inhibition of pyruvate dehydrogenase kinase.

### **Insulin Resistance**

Insulin resistance is commonly present in heart failure even in the absence of diabetes and independent of the cause of heart failure. The failing heart metabolises carbohydrates and FFAs for energy production and insulin resistance compromises this mechanism.

Diabetics have higher systolic blood pressures, higher pulse pressures and longer duration of hypertension than non diabetics. Compared to non-diabetic hypertensives diabetics has decreased stress corrected mid wall shortening.

### **Diastolic dysfunction in Diabetes**

Diastolic abnormalities have been observed in patients with DM, Impaired augmentation of LVEF during exercise occurs in upto 40% of patients Echo studies have demonstrated prolonged IVRT, delayed opening of mitral valve, decreased rate of LV diastolic filling and abnormal transmitral flow velocities. Diastolic abnormalities may be present earlier than and independent from systolic



abnormalities in patients with DM.

Diastolic dysfunction implies elevation of left ventricular end diastolic pressure with normal LV end diastolic volume and normal ejection fraction.

The pathophysiology relating to diastolic heart failure is related to an increase in ventricular filling pressure relative to volume and secondary to either myocardial or pericardial disorders.

Restrictive cardiomyopathy is a broad category of myocardial diseases characterised by decreased passive chamber compliance, usually without significant systolic dysfunction. It can result from various systemic and local disorders.

The addition of Doppler imaging to conventional Doppler Echocardiography demonstrated diastolic dysfunction in 75% of 57 asymptomatic normotensive diabetic patients. TDI detected diastolic dysfunction more often than any other echocardiographic approach.

### **Diastology**

We define diastole as starting with the onset of isovolumic relaxation and ending with the closure of mitral valve. Diastole thus includes isovolumic relaxation period and diastolic filling period. Until recently diastole was considered as a passive portion of cardiac cycle. Within the last few decades there has been a growing realisation that heart failure can occur in the presence of normal systolic function (24).

Using Echocardiography, it is now possible to noninvasively measure chamber dimensions, motion of the mitral annulus, motion of the chamber walls, transmitral and pul. Vein flows and intra cardiac flow (25).

## **Phases of diastole**

### **a) *Isovolumic Relaxation Phase***

In this phase there is no LV filling, but it has an impact on filling of LV in the subsequent phase. This is an active phase and requires lot of energy.

### **b) *Rapid Filling Phase***

Major portion of the ventricular filling occurs during this phase and is governed by myocardial relaxation, mitral valve gradient and myocardial compliance.

### **c) *Slow Filling Phase***

This is dependent on the passive compliance or stiffness of ventricle. Very little filling occurs during this phase.

### **d) *Atrial systole***

The contribution of atrial contraction towards ventricular filling depends on the LV compliance and rhythm of the patient. Normally the atrial contraction contributes upto 15% of LV filling. But if the LV is less compliant the contribution may increase to 30-35%.

Although there are numerous independent factors that affect LV diastolic properties and the filling of LV, all factors work through their combined resultant effects on the transmitral gradient (TMPG) which is the actual physical determinant of LV filling. The effects of two key diastolic properties, the rate of LV relaxation

and LV compliance are especially important in the understanding of LV filling patterns in health and disease.

LV relaxation describes the rate of LV pressure decline during isovolumic relaxation. Quantitation of LV relaxation is done by describing the rate of LV pressure decline during isovolumic relaxation (26). Another key LV diastolic property is the operating chamber compliance ( $dV/dp$ ). This affects the LA and LV filling pressures and is composed of stiffness. The LV chamber stiffness is described by a tangent, the steeper the slope of the tangent the less compliant (Stiffness) is the ventricle.

The TMPG determines the LV filling pattern and is influenced by the speed of LV relaxation and LV compliance. For any given LV pressure, faster LV relaxation results in a larger early TMPG, more filling in early diastole and consequently less filling in late diastole. Conversely, when LV relaxation is slowed, the proportion of early diastolic filling declines and a greater proportion is seen at atrial contraction. Because the rate of LV relaxation and LA pressure is a continuum many different TMPGs and LV filling patterns are possible. Impaired or slowed LV relaxation is the earliest and commonest diastolic abnormality, with a decrease in LV compliance and increase in filling pressures seen in patients with more advanced and symptomatic cardiac disease.

### **Mitral floor velocity variables**

Left ventricular isovolumic relaxation time (IVRT) is the time interval from Aortic Valve closure to mitral valve opening. Longer IVRT values ( $>100$  ms) are associated with impaired relaxation and normal filling pressures. This lengthening of

IVRT interval is the earliest change seen with diastolic dysfunction and is sensitive to slowing of the rate of LV relaxation. A short LV IVRT indicates an earlier mitral valve opening and can be seen in young normal individuals or patients with increased mean LA pressure. (Fig-2)

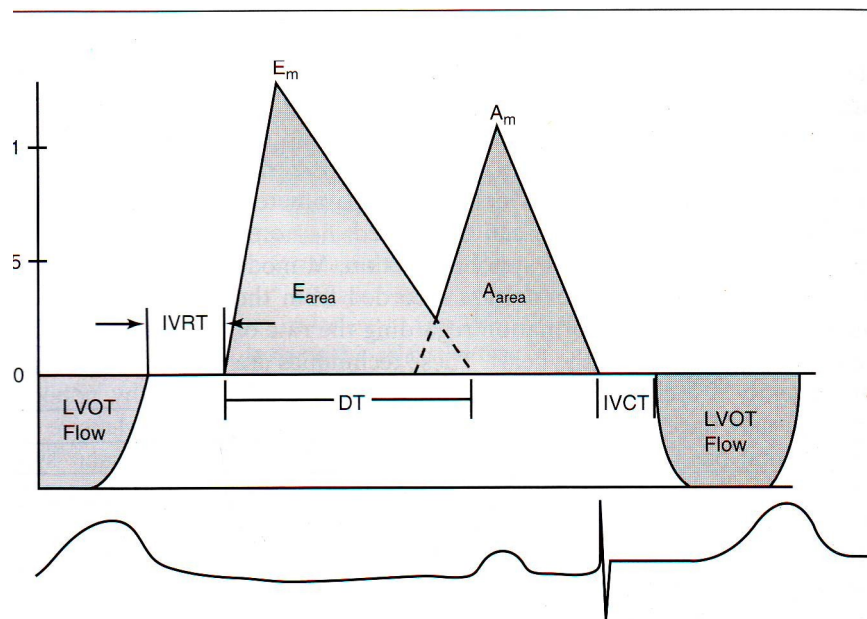
Peak E-wave velocity reflects early diastolic TMPG. Similarly peak mitral A wave velocity reflects the late diastolic TMPG. The overall type of filling pattern is generally characterised by the mitral E to A wave ratio.

#### **Normal Values for mitral flow velocity curves**

E-Velocity	$0.85 \pm 0.16$ m/sec
A-Velocity	$0.56 \pm 0.13$ m/sec
DT	160 - 240 msec
IVRT	70 - 100 msec

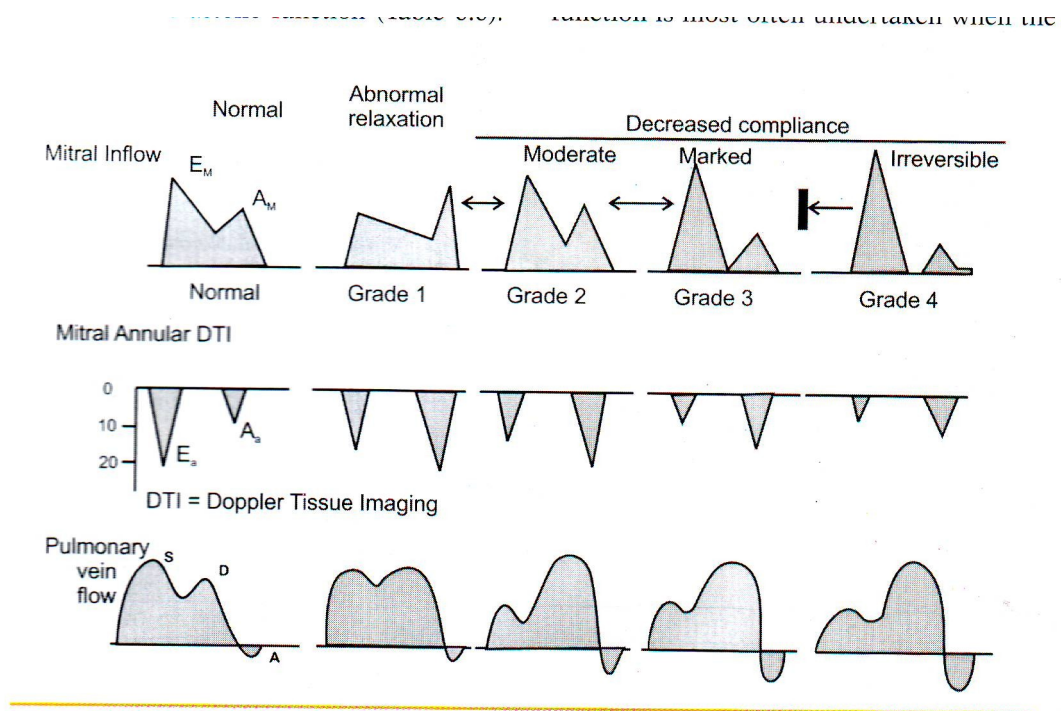
Normal E/A ratio - 1.6.

Fig-1



Different components of mitral valve inflow

Fig-2



Schematic representation of mitral inflow (top) mitral annular Doppler tissue imaging (middle) and pulmonary vein flow (Bottom) in a normal individual in various grades of diastolic dysfunction

Elastic recoil and rapid LV-relaxation in adolescents and young adults results in a predominance of early diastolic filling (E-wave) with much less filling (10-15%) caused by atrial contraction. With normal aging LV systolic function changes little but LV relaxation slows in most individuals. This appears to be caused by an increase in systolic BP and LV mass. The result is reduced LV filling in early diastole and increased filling at atrial contraction. In most individuals the peak E-wave and A wave velocities become approximately equal during the 7<sup>th</sup> decade of life.

### **Abnormal patterns of diastolic dysfunction**

In patients with cardiac disease three abnormal LV filling patterns are recognised. (Fig-2)

The least abnormal and most common is termed impaired relaxation resulting from reduced filling in early diastole, a reduced Mitral E to A velocity ratio, increased A wave amplitude and filling caused by atrial contraction and often on S<sub>4</sub> gallop.

### **Diastolic dysfunction**

1. Abnormal Relaxation pattern
2. Pseudonormalisation
3. Restrictive pattern
  - a. Reversible
  - b. Irreversible

With disease progression the LV compliance become reduced and LA pressure increases which counteracts the impaired LV relaxation. The increased early TMPG results in an LV filling pattern that appears normal but is actually pseudo-normal. This term indicates that despite the normal mitral E to A wave ratio abnormalities of LV relaxation and LV compliance are present. Finally in patients with advanced disease and

**Table 3 : Abnormal Relaxation Pattern**

E-Velocity	<	A Velocity
DT	>	240 m/sec
IVRT	>	100 m/sec
E/A Ratio	<	1

**Table 4 : Pseudo normalisation**

DT		160-200 m/sec
IVRT	<	90 m/sec
E/A		1 - 1.5
PVs <sub>2</sub>	<	Pvd
Mitral A duration	<	Pva duration
Pva	>	35 cm/sec.

a severe decline in LV compliance, the high pressures cause the LV filling to become restrictive with blood rapidly entering a slowly relaxing ventricle in early diastole only to be abruptly decelerated generating an S<sub>3</sub> gallop. With a marked increase in early LV diastolic pressure the Lt atrium is dilated and hypercontractile with little additional filling at atrial contraction. When restrictive pattern is

**Table : Restrictive Pattern**

E Velocity	<	A velocity
DT	<	150 m/sec
IVRT	<	70 m/sec
E/A Ratio		2

observed, increasing E velocity indicates increasing LA pressure and decreasing A wave correlates with increasing LVED pressure.

In early phases this pattern may be reversible by changing the loading conditions of the heart by drugs like nitrites. When it becomes irreversible it indicates end stage of the disease. The patient has dyspnoea at rest or minimal exertion, S<sub>3</sub> is present and prognosis is poor.



## **ECHO-DOPPLER EVALUATION OF LEFT VENTRICULAR DIASTOLIC FUNCTION**

Although a variety of modalities are available to evaluate diastolic dysfunction, Echo-Doppler study has emerged as the modality of choice because of the rapidity with which it gives information, its being non invasive and its repetitiveness.

### **Modalities used to evaluate diastolic function**

1. Echo-Doppler
2. Radionuclide Studies
3. Haemodynamic Studies
4. Tissue Doppler Studies

### **Echo Doppler**

The functional behaviour of the normal and pathologic cardiac chamber can now be assessed non-invasively. Virtually all types of acquired heart diseases are associated with a component of diastolic dysfunction. The diastole comprises 2/3 of cardiac cycle. Lt ventricle diastolic pressure is transmitted to the Lt atrium and to the pulmonary veins for a relatively longer period than in systolic pressure.

Transmission of elevated diastolic pressures to the pulmonary veins can be a substantial driving force in development of pulmonary hypertension. Because diastole comprises two thirds of cardiac cycle, diseases that elevate diastolic pressure are more likely to be associated with secondary pulmonary hypertension

than are diseases with isolated systolic pressure. Diastolic dysfunction is a significant contribution to the development of congestive heart failure. Although there are a number of medical and surgical treatments available for systolic overload of LV like Aortic stenosis, there are fewer options for the treatment of diastolic dysfunction.

There are numerous techniques for evaluation of diastolic dysfunction.

Table-I

Anatomy Level	-	Continuous diastolic volume
Diastolic filling rate		Flow based
		- Mitral
		valve inflow pattern
		E/A Ratio
		Deceleration Time
Isovlumic Relaxation Time		
Dimension less Myocardial Performance Index (MPI)		
		Pulmonary Vein Flow
		<b>Doppler Tissue Imaging</b>
		Mitral annular diastolic velocity
		Mitral valve E-wave / E <sub>A</sub> ratio.

### **M-mode Echo Cardiography**

It plays little role in the evaluation of diastolic function. One M-mode finding that has retained clinical relevance is the presence of B hump of mitral valve closure. It is an indication of elevated diastolic pressure, but it provides no quantity

information.

## **Two Dimension Echo Cardiography**

It is an excellent tool that can identify, characterise and quantify diseases that caused by diastolic dysfunction. The combination of thickened left ventricular walls, Lt atrial dilatation and absence of mitral valve disease is a strong indication for the diastolic dysfunction.

### **Evaluation of Mitral inflow**

Mitral inflow pattern is evaluated from an apical transducer position with sample volume placed at the tip of the mitral valve. Normal mitral inflow consists of a biphasic flow with mitral E-wave exceeds the A wave both in velocity and volume. An additional commonly used measurement is deceleration time of E-wave with delayed LV relaxation, there is prolongation of deceleration time.

### **Determination of IVRT**

IVRT represents Isovolumic Relaxation time (IVRT). This is the earliest part of diastole - It is defined as the time from Aortic Valve closure and mitral valve opening and is  $76 \pm 13$  m/sec in adults. Diseases that result in elevation of left atrial pressure will shorten the IVRT.

### **Myocardial Performance Index (MPI)**

This is derived by comparing the total systolic time from mitral valve closure to mitral valve opening with systolic time involved in actual aortic flow or ejection time. The total systolic time is defined as isovolumic contraction time (IVCT) + Ejection time + IVRT. The MPI is derived as follows.

$$\text{MPI} = \frac{(\text{IVCT} + \text{IVRT})}{\text{ET}}$$

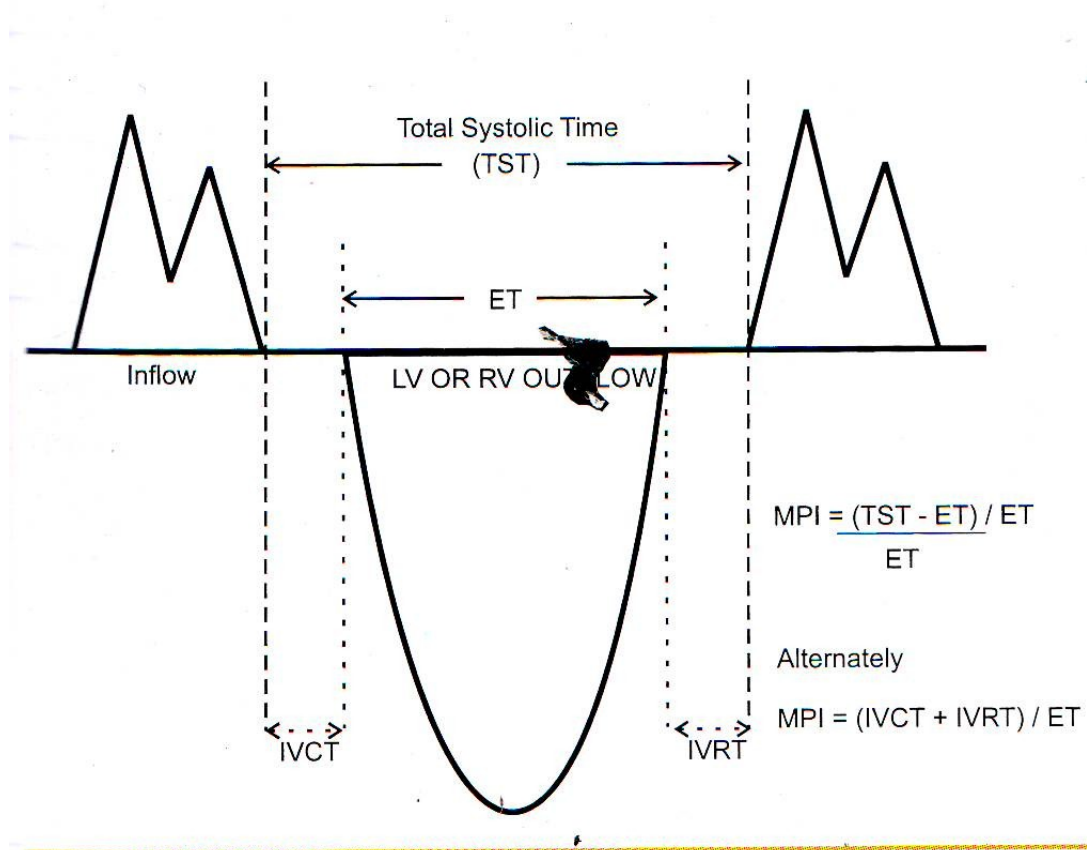
normal MPI is less than 0.40. It combines by systolic and diastolic function.

## TISSUE DOPPLER IMAGING

It is a recently developed ultrasound imaging modality that has underlying physics and principles similar to those of conventional PW spectral Doppler. Instead of blood flow, TDI measures the velocity of myocardium during cardiac cycle. Blood flow is typically low amplitude and high velocity in nature, whereas myocardial velocities are of higher amplitude and low velocity. The limitations of TDI are also similar to standard Doppler in that PW display, while having a high temporal resolution, only measures velocities at a single point within the heart. TDI cannot separate translational and rotational components that also occur with myocardial contraction and relaxation. To minimise this limitation, imaging from the longitudinal axis plane (apical window) is performed. From this view the axial motion of the left ventricle is parallel to the transducer axis and the velocities are primarily related to LV contraction and relaxation. For TDI spectral analysis a 3-7 mm PW sample volume is placed in different segments of LV (such as septum, and lateral, anterior, inferior or posterior walls) and regional quantification of segmental velocities are obtained. The PW sample volume is placed within the septal or lateral regions of the mitral annulus. The TDI function of the ultrasound machine is activated. (Fig-4)

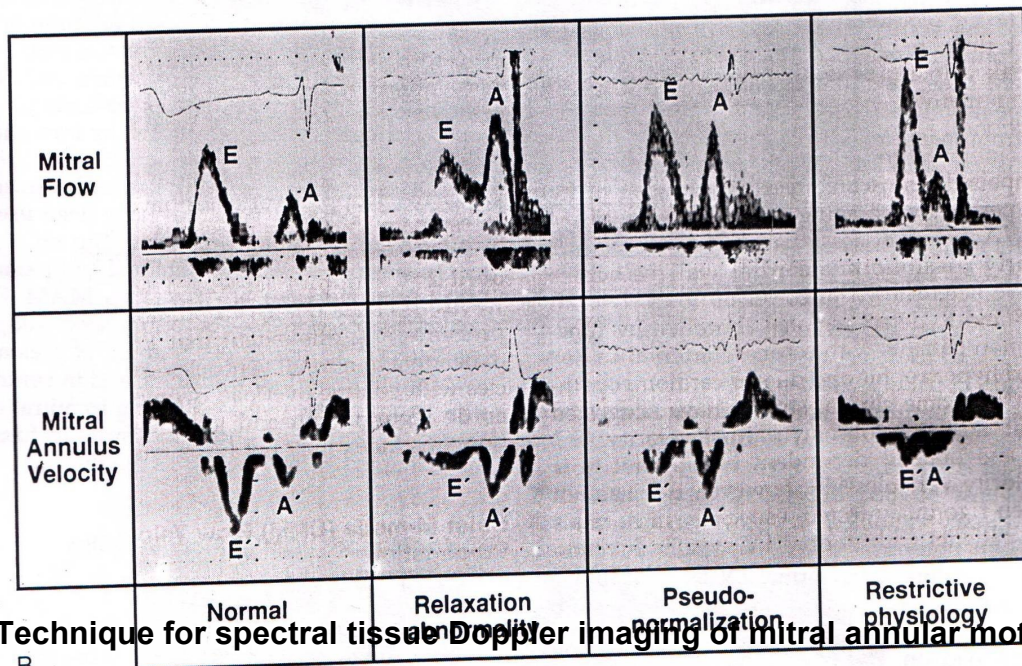
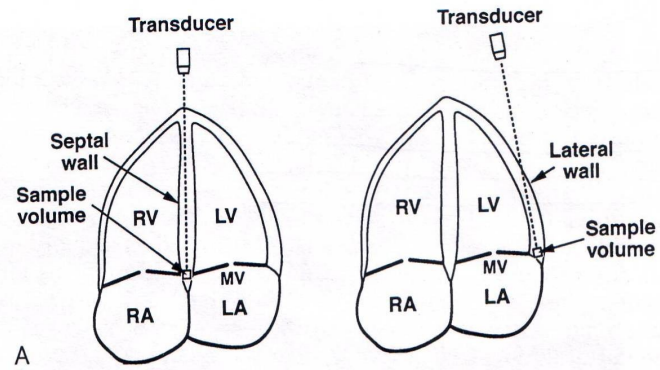
In Sinus Rhythm there are two annular motions ( $E_a$  and  $A_a$ ) In normal disease free state  $E_a$  is greater than  $A_a$  similar to the relationship of mitral E and A waves. With diastolic dysfunction there is reduction in  $E_a$  and the annular  $E_a/A_a$  ratio reverses. The annular velocity is not volume dependent as opposed to mitral inflow.

Fig-3



**Calculation of myocardial performance index (MPI)**

Fig-4



Technique for spectral tissue Doppler imaging of mitral annular motion

R

There is a positive (toward apex) systolic signal ( $S_m$ ) and negative signal in early ( $E_a$ ) and late diastole ( $A_a$ )(27).

Similar to transmitral profiles patients with impaired ventricular relaxation owing to LV hypertrophy or aging often have an MAM.  $E_a/A_a$  ratio of less than 1. (28).

Combined TDI mitral annular and conventional PW Doppler variables have been used to estimate LV filling pressures.

The ratio of early diastolic velocities obtained with standard PW Doppler (E-Wave) to MAM  $E_a$  wave have been related to pulmonary wedge pressures. Various investigators have used  $E/E_a$  ratios of 10, 12 or 15 to stratify pulmonary capillary pressures exceeding thresholds of 18-20 mmHg. An elevated  $E/E_a$  ratio has been associated with poor prognosis in both ischaemia and non-ischaemic left ventricular dysfunction.

### **Colour Doppler M-mode imaging**

For evaluation of diastolic function mitral inflow propagation velocity is evaluated from LV apex. This technique can document reduced flow velocities that are manifest as a reduced slope of colour Doppler-M-mode signal. In normal situation there is a rapid slope implying high velocity of flow. In diastolic dysfunction, the velocity of early filling is reduced and organized propagation of flow does not occur past the midventricle.

### **Left atrial Volume / Size**

Several recent studies have shown the prognostic importance of measuring Lt atrial size. Lt atrial size is an indirect marker of LV diastolic dysfunction.

## PULMONARY VEIN FLOW

As with mitral flow velocity, Pul.Venous velocity changes with normal aging and disease states. With experience high quality PW Doppler transthoracic recordings can be obtained in approximately 85% to 90% of patients. The haemodynamic determinants of Pul. Venous flow velocity recently have been studied in vivo. This include peak flow velocity in early systole (PVS<sub>1</sub>) late systole (PVS<sub>2</sub>) and early diastole and peak reverse flow velocity at atrial contraction and its duration. (PVa dur)

PVS<sub>1</sub> occurs as a result of LA relaxation and pressure decrease. PVS<sub>2</sub>, which peaks later in systole reflects the interaction of RV stroke volume, LA pressure and compliance. Pul. Venous diastolic flow velocity (PVd) initially follows early diastolic mitral flow velocity, but in mid diastole LV filling slows, whereas PVd flow continues with ongoing LA enlargement.

Pulmonary venous flow reversal owing to atrial contraction (PVa) is determined by LA contractility and compliance of the pulmonary venous bed, LA & LV. Pulmonary venous flow velocity patterns can be matched to their corresponding mitral Doppler patterns. Pul. venous systolic to diastolic flow velocity ratios help determine the type of LV filling pattern. The relation between pulmonary Pul. Venous A wave and mitral A wave duration is of special importance (29). When accurately recorded, this relation is an important age-dependent indication of La wave pressure increase and LV and diastolic pressure.

Simply stated, when the LA contracts the net volume and duration of flow under normal conditions should be greater, flowing forward into LV rather than backward into Pul. Vein. If pulmonary venous A wave is increased either in velocity (>35 cm/sec) or duration > 30 msec longer than mitral A wave duration, LV A-wave



pressure is increased and end-diastolic pressure is elevated.

Typically, imaging is performed from the apical view. The Rt pulmonary vein is most easily visualized. The sample volume can be placed at the orifice of Pul vein and PW Doppler imaging is used to record the flow envelope. With increasing stiffness and decreasing compliance of LV, emptying of the Lt. atrium becomes incomplete during diastole. Because of this, at the onset of systole, the Lt atrial volume and pressure are elevated. This results in a reduction of flow volume into the left atrium from Pul veins during ventricular systole.

The pulmonary A wave duration can be compared with the mitral A wave duration. Evaluation of Pul. Venous flow can give valuable clue to the presence of pseudonormalisation, when a normal mitral inflow E/A ratio has been noted in a situation in which diastolic dysfunction is likely. In this instance, the pul vein flow will reveal blunted systolic velocities and relatively greater diastolic inflow with accentuation of A wave.

Renee L. Bess et al conducted a study to determine which Doppler parameters could be most successfully obtained. They concluded that MV flow and TDI annular velocities can be recorded in virtually all patients, require the least time to record and demonstrate low inter-reader variability (30).

So in this study we have selected MV flow, TDI annular velocities and pulmonary venous flow studies to evaluate our patients. The success rate in MV flow and TDI was 100% and Pulmonary venous flow 85%.

**Table II****European study group of diastolic heart failure guidelines (18)**

E/A < 50 yrs < 1 and DT > 220 m/sec.

E/A > 50 yrs < 0.5 and DT > 50 years > 280 m/sec.

S/D < 50 yrs > 1.5 S/D > 50 years > 2.5 m/sec.

1 VRT < 50 yrs > 92 m/sec IVRT 30-50 yrs > 100 m/sec.

I VRT > 50 yrs > 105 m/sec.

PVA velocity > 35 cm/sec.

## MATERIALS AND METHODS

Patients were selected consecutively from those attending as outpatients to the Diabetic clinic attached to Govt. Stanley Hospital, Chennai - 1. 89 patients were selected initially. A thorough clinical examination was made to rule out the presence of any diseases. BP was recorded for 3 days in all the patients and BP reading  $> 130/85$  on any one occasion were excluded from the study. Patients with other medical illnesses were excluded. Height and weight were recorded in all the patients. Resting ECGs were taken for all patients. Patients with abnormal ECGs were excluded. Random blood sugar was estimated in all the patients. Fasting blood sugar was estimated the next day. By this process 39 patients were excluded from the study.

Since CAD, hypertension, peripheral vascular diseases were commonly associated with diabetes these patients were screened for them. Urine analysis and renal function tests were done in all the patients. Ophthalmological opinion was obtained whenever necessary. TMT was done in all patients and those with positive TMT test were excluded.

The study period was from January 2007 to December 2007. 50 patients were selected. There were 34 males and 16 Females.

All the selected patients fulfilled the following criteria.

1. Type II Diabetes Mellitus
2. Duration of DM  $> 5$  years
3. Under Regular Treatment

4. Age below 55 years.

**Exclusion Criteria**

1. Blood pressure > 130/85.
2. Abnormal Resting Electro Cardiogram
3. Positive Tread Mill Test for inducible ischaemia.
4. Patients with micro vascular or macro vascular complications of diabetes.
5. Patients above 55 years of age.

The effect of age on the diastolic function is known. So the upper age of the study group is arbitrarily fixed at 55 years.

The diagnosis of diabetes was established according to the current WHO criteria. Tread mill tests were done by cardiologists who were blinded to Echocardiographic diagnosis. Both treadmill test and Echocardiography were done on the same day.

Body mass Index was calculated as weight in kilograms divided by squared height in meters.

Twenty healthy subjects drawn from attenders of patients served as control group.

Prior approval from institutional ethic committee was obtained and all subjects gave written informed consent.

**TREADMILL TESTING**

All subjects including controls did the same symptom limited graded exercise test on a treadmill. Bruce Treadmill protocol was applied to all patients. Time in seconds on the Tread mill was used to evaluate exercise capacity and number of metabolic equivalents (METs) was estimated. Blood pressure was recorded with a manual mercury sphygmomanometer. BP and Heart rate was recorded every 3 minutes. An average 12 lead electro cardiogram monitored cardiac status during the exercise test.

### **Echocardiography**

All subjects including controls underwent Echo evaluation. They were examined in the left lateral decubitus position using standard views. Studies were done using an ALOKA SSD 4000 phased array system equipped with tissue Doppler and harmonic imaging technology. Parasternal long axis, parasternal short axis as well as apical 4 chamber, five chamber and two chamber views were used for the evaluation of functions of left ventricle and the heart valves. LV dimension and fractional shortening (FS) of left ventricle were calculated by using Teicholtz formula. Ejection fraction was obtained by modified Simpsons' method.

Pulsed wave Doppler measurements of mitral inflow were obtained with the transducer on the four chamber view with a 1-2 mm Doppler sample volume placed between the tips of the mitral leaflets during diastole. The left ventricular outflow velocity curve was recorded from the apical five chamber view with the sample volume positioned just below the aortic valve.

Doppler velocities and time intervals were measured from mitral inflow and left ventricular outflow recordings. Isovolumic relaxation time (IVRT) was the time interval from the cessation of left ventricular outflow to the onset of mitral inflow. Ejection time was the time interval from the onset and cessation of left ventricular

outflow. Deceleration time (DT) was the time interval between the peak E velocity and the end of the early diastolic flow. Total systolic time interval was measured from the cessation of one mitral flow to the beginning of the following mitral inflow. Isovolumic contraction time (IVCT) was calculated by subtracting ET and IVRT from total systolic time interval.

Tissue Doppler echo was performed by activating the tissue Doppler function in the same machine. Images were obtained in the apical 4 chamber view with the filter setting were kept low and gains were adjusted at the minimal optimal level to minimize noise. 1.7 mm sample volumes were placed at both septal and lateral mitral annular site and systolic velocity ( $S_m$ ) early and late diastolic velocities ( $E_m$  or  $E^1$ ,  $A_m$  or  $A^1$ ) were obtained and average values were taken.  $E/E^1$  ratio was calculated. TDI was less sensitive to preloading conditions (31).

Pulmonary venous flow recordings were obtained from apical 4 chamber view with the sample volume positioned 1-2 cm into the right upper pulmonary vein and following measurements taken.

- Peak S-wave inflow velocity (cm/sec) during ventricular systole.
- Peak D-wave inflow velocity (cm/sec) during early phase of ventricular diastole and corresponding S/D ratio.
- Peak reversed A-wave (PVA) velocity (cm/sec) during atrial contraction.

Although all echo Doppler indices remain imperfect and much remains to be learned the aggregate sum of this information remains our best and most practical way to assess diastolic function, and to objectively follow serial changes after medical intervention or with disease progression.(32)

Combined TDI mitral annular and conventional PW Doppler variables have been used to estimate LV filling pressures. The ratio of early diastolic velocities obtained with standard PW Doppler(E-wave)to MAM Em waves have been related to pulmonary wedge pressures.(33)

Despite epidemiologic observations of greater frequency of heart failure in diabetic subjects and credible explanations for LV Dysfunction, some studies in diabetic patients without overt evidence of heart disease have demonstrated normal contraction at rest. In these circumstances the contractile response during exercise was abnormal suggesting loss of contractile reserve in early phase of diabetic heart disease. In this situation the resting changes may be too subtle to be identified with load dependent indicators like ejection fraction, and require the application of sensitive techniques(35).

## **STATISTICAL ANALYSIS**

Datas are expressed as mean value  $\pm$  standard deviation (SD) statistical significance was defined as  $P < 0.05$ . Statistical analysis was done by using SPSS software system.

## RESULTS AND ANALYSIS

The total number of subjects were 50. The number male patients is 34 (68%) and female patients were 16 (32%). The age group ranges from  $46.7 \pm 7$  Average length of the duration of diabetes is  $7.5 \pm 0.8$  years. All patients have normal LV systolic function.

**Table III**

### Demographic characteristics of diabetic patients

Age - years	$46.7 \pm 7$
Body mass Index	$24.5 \pm 0.65$
Male Gender	68%
Female Gender	32%
Systolic Pressure mm Hg	$118.5 \pm 1.8$
Diastolic pressure mm Hg	$72.5 \pm 1.5$
Length of time since the diagnosis of DM	$7.5 \pm 0.8$

Diastolic dysfunction was present in 18 patients (36%) through conventional Echo. 14 patients (28%) have diastolic dysfunction through TDI.

The group (18 patients) that was diagnosed as having diastolic dysfunction by conventional method differs from the group without diastolic dysfunction only on two aspects - IVRT and PVa velocity. But the group identified by TDI have clear cut differences in several parameters, like Em velocity, Am velocity, Em/Am ratio, IVRT, LA diameter and septal wall thickness. This shows the relative insensitivity of conventional Echo Doppler methods in diagnosing diastolic dysfunction.



Table IV

**Comparative study of diastolic dysfunction group  
and without diastolic dysfunction**

	Diastolic Disfunction				Student independent t-test
	No		Yes		
	Mean	SD	Mean	SD	
FBS	131.10	23.89	154.39	34.39	t=2.65 P=.01 significant
METS	12.39	2.10	10.52	2.82	t=1.19 P=0.003 significant
EF	68.22	7.51	64.21	5.65	t=2.37 P=0.002 significant
lv_mass	78.92	2.15	82.45	2.97	t=3.31 P=0.001 significant
LA-diameter	33.50	1.92	34.87	2.25	t=2.30 P=0.03 significant
Lv_dias_diameter	50.56	2.96	51.00	3.41	t=0.49 P=0.62 not significant
SEPTAL WALL THICKNESS	7.56	1.15	7.98	1.32	t=1.21 P=0.22 not significant
E_A_ratio	1.34	.21	1.28	.44	t=0.63 P=0.53 not significant
dt	163.67	38.74	211.29	61.54	t=3.07 P=0.003 significant
pva	27.40	5.11	31.91	7.34	t=2.19 P=0.03 significant
S_D_ratio	1.06	.18	.98	.48	t=0.65 P=0.52 not significant
Em	13.72	2.97	13.06	5.37	t=0.49 P=0.62 not significant
Am	9.72	2.49	11.25	2.74	t=2.08 P=0.04 significant
Em/Am	1.41	.32	1.19	.53	t=1.71 P=0.09 not significant
E/Em	8.22	1.96	7.12	2.52	t=0.83 P=0.41 not significant

Fasting blood sugar levels are significantly elevated in the group with diastolic dysfunction. But there is no significant variation between those with diastolic dysfunction by TDI or conventional methods.

Among 18 patients identified by Conventional Echo Doppler to have diastolic dysfunction, 3 patients had Grade II diastolic dysfunction. These 3 patients were identified both by TDI and conventional Echo Doppler. The E/A Ratio was >

1,  $DT > 200$  MS and  $IVRT < 90$  msec and  $PVA$  velocity  $> 35$  cm/sec.  $PVa$  Velocity  $> 35$  cm/sec confirms that the patients have only Grade II diastolic dysfunction.

All patients identified by TDI have  $Em/Am$  Ratio  $< 1$  and  $Em$  velocity  $< 8.5$  cm/sec, clearly indicating diastolic dysfunction. These findings clearly show that tissue Doppler imaging is superior in the early diagnosis of diastolic dysfunction in diabetics. TDI is also more sensitive method.

10 patients have diastolic dysfunction both by conventional method and TDI. In these patients the  $EA$  ratio was  $< 1$  in 7 patients and  $PVa$  velocity was  $> 35$  cm/sec in all the patients. TDI parameters of LV diastolic dysfunction ( $Em/Am$  ratio  $< 1$  and  $Em$  velocity  $< 8.5$  cm/sec) was present in all the patients. This again shows that TDI can pick up individuals with diastolic dysfunction from among individuals in whom the conventional parameters for the diagnosis of diastolic dysfunction was varying.

### **Comparison between diastolic dysfunction group and without diastolic dysfunction (Table III)**

The fasting blood sugar is significantly elevated in the diastolic dysfunction group ( $t=2.65$   $P=0.01$  significant). The diastolic dysfunction group shows a decline of about 15% exercise capacity. LV mass is significantly elevated in diastolic dysfunction group ( $t=3.31$   $P=0.001$  Significant) Ejection fraction is significantly decreased in diastolic dysfunction group when compared to group without diastolic dysfunction. There is significant increase in the LA diameter in the diastolic dysfunction group ( $t=2.30$   $P=0.003$  Significant).

Reduction in  $E/A$  Ratio is not significant.

Other diastolic function parameters like  $DT$ ,  $PVa$  and  $Am$  are significantly

elevated in Diastolic dysfunction group. Other variable like Lv diastolic diameters, septal wall thickness, S/D ratio Em/Am ratio do not show significant differences.

SARAIVA ET AL showed in their study that Tissue Doppler Imaging can identify asymptomatic diabetics with diastolic dysfunction. In their study both Echo Doppler and TDI were employed to evaluate diastolic dysfunction. Tissue Doppler imaging identified diastolic dysfunction in 26.6% of diabetics, while the classical criteria did so in 40.5% of the cases. The group identified by classical criteria did not differ significantly from patients without diastolic dysfunctions, while in the group identified by TDI significant differences were highlighted. These findings are nearly similar to our findings. Their study showed close correlation between these groups with regard to LV mass index whereas our study does not find any correlation in this aspect.

Savaiva Et al concluded in their study justifying the use of TDI for the assessment of diastolic dysfunction with otherwise healthy hearts(15).

#### **Comparison between study group and controls (Table IV)**

There are significant differences between these two groups. This is only as expected. The fasting blood sugar (FBS) is much elevated in the study group. There is a 21.4% reduction in exercise tolerance in diabetics compared to controls. The E/A ratio is significantly decreased in the study group than the control group. There is 26% increase of deceleration time in diabetic group when compared to controls. Pulmonary venous atrial reversal velocity is significantly increased in diabetics as a group. S/D ratio is significantly reduced. 16% increase in IVRT was noted in Diabetic group. Other diastolic functional parameters like Em, Am, Em/Am, E/Em ratios show significant differences in these two groups.

**Table V**

**Echocardiographic characteristics of groups with diastolic dysfunction identified by conventional and TDI methods.**

	con_tiss	N	Mean	Std. Deviation	Student independent t-test
FBS	Conv TDI	18 14	151.61 156.93	17.584 25.281	t=0.70 P=49 not significant
METS	Conv TDI	18 14	10.671 9.118	2.5341 1.6718	t=1.35 P=0.03 significant
EF	Conv TDI	18 14	65.44 66.14	6.271 5.749	t=0.32 P=0.75 not significant
lv_mass	Conv TDI	18 14	81.42 83.33	2.360 3.771	t=1.76 P=0.09 not significant
LA-diameter	Conv TDI	18 14	33.89 35.71	1.779 1.899	t=2.79 P=0.01 significant
Lv_dia_diameter	Conv TDI	18 14	51.39 50.79	3.466 3.766	t=0.47 P=0.64 not significant
SEPTAL WALL THICKNESS	Conv TDI	18 14	7.72 8.64	1.227 1.216	t=2.11 P=0.04 significant
E_A_ratio	Conv TDI	18 14	1.061 1.121	.4060 .4246	t=0.41 P=0.69 not significant
dt	Conv TDI	18 14	257.06 226.93	56.637 52.305	t=1.54 P=0.13 not significant
pva	Conv TDI	18 13	35.22 35.00	3.388 7.735	t=0.11 P=0.91 not significant
S_D_ratio	Conv TDI	18 13	1.02 .80	.646 .387	t=1.07 P=0.29 not significant
Em	Conv TDI	18 14	12.00 7.14	2.970 .864	t=5.91 P=0.001 significant
Am	Conv TDI	18 14	10.22 12.50	2.290 2.345	t=2.76 P=0.01 significant
Em/Am	Conv TDI	18 14	1.211 .552	.4861 .1173	t=4.94 P=0.001 significant
E/Em	Conv TDI	18 14	7.417 8.779	2.8932 1.8082	t=1.54 P=0.13 not significant
IVRT	Conv TDI	18 14	111.50 99.24	16.797 17.323	t=2.02 P=0.05 significant

**Table V-A**

### Group-Sex Cross Tabulation

Count

		Sex		Total
		Male	Female	
Group	Study	34	16	50
	Control	16	4	20
Total		50	20	70

$\chi^2 = 1.01$  P=0.32 not significant

There were 34 males and 16 females in the study group and 16 males and 4 females in the Control Group. The difference in the numbers between males is statistically not significant.

**Table V-B**

**Sex\*con-tdi**

		con_tdi		Total
		Conv	TDI	
Sex	F	8	3	11
	M	10	11	21
Total		18	14	32

$\chi^2 = 1.85$  P=0.17 not significant

Among the females 8 were identified to have diastolic dysfunction by conventional method and 3 patients by TDI. But 10 males were identified to have diastolic dysfunction by conventional method and 11 males by TDI method. However this difference is not statistically significant.

Table VI

Comparison between Echocardiatic characteristics of study group and controls

	Group				Student independent t-test
	Study		Control		
	Mean	SD	Mean	SD	
FBS	154.10	22	94.55	13	t=11.3 P=0.001 significant
METS	10.90	2.5	13.87	1.8	t=4.85 P=0.001 significant
EF	66.64	7	61.75	4	t=3.07 P=0.003 significant
lv_mass	891.05	3	80.16	2	t=1.13 P=0.26 not significant
LA-diameter	34.26	2	35.15	3	t=1.51 P=0.13 not significant
Lv_dias_diameter	50.92	3	50.80	3	t=0.13 P=0.89 not significant
SEPTAL WALL THICKNESS	7.92	1	7.75	1	t=0.49 P=0.62 not significant
E_A_ratio	1.18	.4	1.58	.3	t=4.33 P=0.001 significant
dt	215.00	63	159.15	20	t=3.85 P=0.001 significant
pva	32.61	6	24.23	5	t=4.29 P=0.001 significant
S_D_ratio	.97	0	1.10	0	t=0.98 P=0.001 significant
Em	11.26	4	18.15	4	t=6.97 P=0.001 significant
Am	10.68	3	11.30	3	t=0.85 P=0.001 significant
Em/Am	1.10	.5	1.60	.2	t=4.38 P=0.001 significant
E/Em	8.09	2.3	5.69	1.7	t=4.14 P=0.001 significant
INRT	101.45	20	83.60	8	t=3.70 P=0.001 significant

Although there is increase in LV mass, LV diastolic diameter and septal wall thickness in the study group as a whole, it is not statistically significant. This is important because there is significant increase in these variables in the diastolic dysfunction group and this indicates the increase in LV mass index is mainly seen in those with diastolic dysfunction.

**Table VII-A**

	Group				Student independent t-test
	Study		Control		
	Mean	SD	Mean	SD	
Age	46.70	7	43.75	7.1	t=1.58 P=0.001 not significant
bmi	25.53	4.9	24.10	1.9	t=1.25 P=0.001 not significant

Comparison of body mass index among male and females is not statistically significant both among study group and control group.

Body mass Index variation in patients with conventional and TDI group is not statistically significant.

**Table VII-B**

	<b>con_tiss</b>	<b>N</b>	<b>Mean</b>	<b>Std. Deviation</b>	<b>Student independent t-test</b>
bmi	Conv	18	26.644	2.7509	t=0.70 P=91 not significant
	TDI	14	24.743	1.9559	

## DISCUSSION

The study group consists of 50 patients. None of them have systolic

dysfunction. 18 patients were identified by to have diastolic dysfunction by conventional echo Doppler method and 14 by TDI method. But in the group identified by conventional Echo Doppler method, not all parameters were full filled. The E/A ratio is normal in most of the patients. But these patients were identified to have diastolic dysfunction on the basis of prolonged IVRT and PVA velocity. But in TDI group, all 14 patients fulfilled both criteria for diagnosis (E'/A' ratio less than 1 and E' velocity less than 8.5 cm/sec). More over the group identified by conventional Echo Doppler method differs very little from those patients without diastolic dysfunction. The exercise capacity of the patients identified by TDI shows a reduction of 17% when compared to those without diastolic dysfunction.

Together with diastolic dysfunction and absence of systolic dysfunction, these are required items by the guidelines of the European study group on diastolic heart failure for the formulation of diastolic heart failure. There were 36% prevalence of diastolic dysfunction in our study according to the above mentioned guide lines. The majority of patients were by IVRT and PVA velocity. Whereas there are a number of guidelines for the diagnosis of Diastolic dysfunction, the reliability of diagnosing diastolic dysfunction on the be basis of only 2 parameters (IVRT & PVA) is in doubt, on the other hand, the group identified by TDI has bold differences from the no-diastolic dysfunction group like decreased Em/Am ratio, prolonged IVRT, decreased Em and increased LA diameter.

Other studies have reported diastolic dysfunction prevalence in diabetes according to tissue Doppler imaging criteria.

VINEREANU ET AL studied patients with Type II DM, recorded the Em velocity at the lateral mitral annulus level. They described that 29% of the patients presented a lateral Em velocity inferior to 8 cm/sec. However they included patients with hypertension. In our study patients with hypertension were excluded and 28% of patients had septal Em velocity less than 8.5 cm/sec. (34)



Another study evaluated the septal annulus Em and Am myocardial velocities and found a prevalence of 78% of Em/Am ratio  $< 1$  in diabetics without left ventricular hypertrophy. High prevalence of hypertension among diabetics together with higher age of the sample may be responsible for such high figures and as such cannot be compared with our study. We have excluded hypertension and patients with age  $> 55$  years.

Boyer JK et al demonstrated in type II DM non-motensive patients a prevalence of 75% diastolic dysfunction, using as diagnostic criteria the presence of both septal and lateral Em velocity less than 8 cm/sec.(36)

Our study showed a reduced exercise capacity in diabetic subjects with diastolic dysfunction. The reduction is 15%. There is positive correlation between METS and E/A ratio. There is negative correlation between DT (deceleration time) and METS. There is also positive correlation between Em/Am ratio. Such correlation has been reported by others also.

A modest correlation between septal myocardial velocity and exercise duration in diabetes has also been recently reported. Diabetics with diastolic dysfunction assessed by tissue Doppler imaging had both E/A and Em/Am ratios correlated inversely with age. Patients identified with diastolic dysfunction by TDI presented with high LV mass index and higher LA diameter and septal wall thickness. Significantly there is insignificant increase in LV diastolic dimensions.

There appears to be no correlation between metabolic control and diastolic dysfunction.

We have found out that there is a higher E/Em ratio in diabetics with diastolic dysfunction diagnosed by TDI. There is a negative correlation between Em

septal myocardial velocity and LA diameter. These findings signal to the presence of higher LV filling pressures in diabetics with diastolic dysfunction.

Diabetic myocardial changes may be due to metabolic derangements, microvascular disease and myocardial fibrosis. The most prominent histopathologic changes in diabetic patients without CAD and hypertension are myocellular hypertrophy and myocardial fibrosis. As hypertension and LVH frequently co exist with diabetes, we studied patients without hypertension and LVH.

Chronic abnormalities in myocardial carbohydrate and lipid metabolism due to insulin deficiency may result in reduced adenosine triphosphatase activity, decreased ability of sarcoplasmic reticulum to take up calcium.

Zhi You Fang et al demonstrated that peak strain rate were significantly reduced in patients with diabetes mellitus and that these changes were analogous to those associated with LVH.

## CONCLUSION

The following conclusions were derived from our study.

1. Diastolic dysfunction is present in asymptomatic diabetics.
2. Conventional Echo Doppler is a relatively insensitive method in the diagnosis of early diastolic dysfunction.
3. Tissue Doppler imaging can identify diastolic dysfunction more accurately than conventional Echo Doppler method.
4. The reduced exercise tolerance in diabetics with diastolic dysfunction recognized by tissue Doppler imaging suggests a potential clinical application for tissue Doppler imaging in the assessment of diastolic dysfunction in normotensive diabetics apparently free from heart disease.
5. In this study, we found out that tissue Doppler imaging is able to unmask the presence of diastolic dysfunction in asymptomatic type II diabetics under-scoring its relation to reduced exercise tolerance, a well recognized ominous prognostic marker. Conversely classical criteria based on PW Doppler do not seem to have the same ability.

## LIMITATIONS OF THE STUDY

All the patients are on oral hypoglycaemic agents. Average fasting blood sugar was 154 mg%. It shows most of the patients have imperfect and unsuccessful control of blood sugar. A greater spectrum of control might have facilitated in establishing a relationship between myocardial dysfunction and glycaemic control.

Exclusion of an ischaemic contribution was mainly based on a normal resting ECG, normal TMT and absence of RWMA in 2D-echo. This does not exclude the possibility of CAD, because of the possibility of false negative results. But such false negative results are usually associated with mild disease and as such it seems unlikely that a major ischaemic contribution was present. This limitation is unavoidable because it would be difficult to justify coronary angiography in asymptomatic diabetic patients on ethical grounds.

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